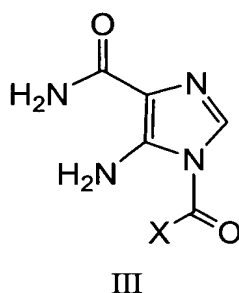


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Filed: JANUARY 16, 2002

wherein R is an alkyl group having from 1 to 6 carbon atoms, comprising,
reacting a compound of the formula III:



wherein X is a leaving group, with an alkylhydrazine having from 1 to 6 carbon atoms.

REMARKS

Claims 1-28 are pending in the application, all of which stand rejected for the reasons of record. The applicant notes the entry of the amendments of Claims 4, 6, 7, 9, 10, 15, 21, 22 and 24 into the record by the Examiner.

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner maintained the rejection that Claim 1 is indefinite as it recites "a time sufficient enough to produce a compound of formula IA". The Examiner stated that it is vague and unclear as to what is the sufficient time and this rejection is same as made in the previous office action.

In response, applicant has amended claim 1 to delete the objected term "a time sufficient enough to produce a compound of formula IA." Accordingly, applicant respectfully requests the withdrawal of this rejection.

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The Examiner stated that Claim 1 is also vague and unclear as to whether the term "iodide" in the inert medium also included or excluded the iodide that can be used as an oxidizing/cyclicizing agent.

In response, applicant has amended claim 1 to state that iodide, by itself, can be used as the oxidation/cyclization agent when there is no other iodide present in the reaction. Support for this amendment can be found on page 8, lines 1-17, where the oxidation/cyclization of formula II into formula IA has been taught with or without the presence of iodide, and further, where the oxidation/cyclization of a compound of formula II is performed using iodide as the oxidizing/cyclicizing agent. Accordingly, applicant respectfully requests the withdrawal of this rejection.

The Examiner stated that the recitation of "inert medium" in claim 1, renders the claim indefinite, as there is no definition of this term in the specification.

In response, applicant has amended claim 1 to delete the term "medium" and has replaced it with an "organic solvent", so that the claimed process utilizes an "inert organic solvent." Support for the amendment of claim 1 can be found on page 8, lines 18- 23, and on page 9, lines 15-16, where the term "inert organic solvent" is defined. Accordingly, applicant respectfully requests the withdrawal of this rejection.

The Examiner maintained that Claim 3 remains indefinite as to the definition of Z, which is recited as (H, Hal).

In response, applicant states that one of ordinary skill in the art would recognize that -NH_2 is capable of being oxidized to form groups such as -NHCl , -NHBr , -NHI , -NCl_2 , -NBr_2 or -NI_2 . Support for this can be found on page 8 of the specification. Accordingly, applicant respectfully requests the withdrawal of this rejection.

The Examiner stated that the recitation of "a reagent that oxidizes NH_2 to NZ " in claim 3 is indefinite as one trained in the art would not know which amino group is being referred to.

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In response, applicant respectfully points the Examiner to the language in claim 3 which states that the "reagent that oxidizes NH_2 to NZ " is a member of the group of oxidation/cyclization agents listed in claim 3. The oxidation and cyclization of formula II to formula IA is claimed in claim 1, described in Scheme III of the specification (page 8, top), as well as page 8, lines 3 to 28 of the specification. Applicant respectfully suggests that it would be clear to one of ordinary skill in the art that the NH_2 group adjacent to the $-\text{N-R}-$ group is the specific $-\text{NH}_2$ involved in the oxidation of NH_2 to NZ and subsequent cyclization. Accordingly, in light of these comments, applicant respectfully requests the withdrawal of this rejection.

The Examiner stated that Claims 10, 16 and 25 are deemed as indefinite as it is not clear what is included or excluded in the X and Y definition.

In response, applicant has cancelled claims 25 and 28, thus obviating those rejections. With regard to claims 10 and 16, applicant respectfully suggests that it would be clear to one of ordinary skill in the art that any number of leaving groups could be used for both X and Y. Examples of proper leaving groups, including those that activate adjacent carbonyl groups, can be found on page 9 (lines 5-15) and page 10 (lines 1-15) of the specification. However, in an effort to advance the prosecution of this case, applicant has amended claim 16 to remove the language "of the type that activates its adjacent carbonyl group towards nucleophiles." Accordingly, in light of these comments, applicant respectfully requests the withdrawal of this rejection.

Claim Rejections - 35 USC § 112, First Paragraph

The Examiner stated that Claims 1-8 and the specification are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for $\text{Bu}_4\text{I}/\text{H}_5\text{IO}_6$ as oxidizing/cyclizing agent, does not reasonably provide enablement for any or all oxidizing/cyclizing agent generically embraced in the claim language (citing In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546). The factors are listed below. 1) The nature of the invention, 2)

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the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

In response, applicant respectfully traverses the above rejection and presents the following comments. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art **without undue experimentation**. See generally, *In re Wands*, 858 F.2d 731, 737, 8 USPQ.2d 1400, 1404 (Fed. Cir. 1998) which includes the incorporation of the 8 factors recited in *Ex Parte Foreman* 230 USPQ 546 (Bd. Of App. and Inter. 1986). Citing prior case law, the Federal Circuit noted in *Spectra-Physics Inc. v. Coherent Inc.*, 827 F.2d 1524, 3 USPQ.2d 1737 (Fed. Cir. 1987) that a specification may, within the meaning of 35 U.S.C. Section 112, first paragraph, contain a written description of a broadly claimed invention without describing all species that claim encompasses. Furthermore, the courts have pointed out that "[n]ot every last detail [of an invention need] be described [in a patent specification], else patent specifications would turn into production specifications, which they were never intended to be." *In re Gay*, 309 F.2d 769, 774, 135 USPQ 311, 316 (C.C.P.A. 1962). The mere fact that experimentation may be complex in the field does not necessarily make it undue, if the art typically engages in such experimentation (quoting from MPEP 2165.01). In the instant case and as acknowledged by the Examiner, applicant has provided working examples oxidation/cyclization reagents such as, periodic acid (H_5IO_6) and BuI_4 , for example, which selectively oxidize the correct amino groups, thus satisfying the enablement requirement.

Further, numerous additional examples of oxidation reagents have been provided on page 8 of the specification. Applicant respectfully suggests that the page 8 examples of reagents satisfy the enablement requirement by providing a more than adequate road map to enable one of ordinary skill in the art to

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practice the invention without undue experimentation. Applicant also respectfully suggests that it would be mere routine experimentation to one of ordinary skill in the art to practice the invention to screen (use) reagents suitable for use as stated on page 8 of the specification. As mandated by the court decisions in Wands, Gay, *etc.*, the applicant is not required to provide examples of all species of oxidation/cyclization reagents.

With regard to the Examiner's statements that the prior art provides no basis for one of ordinary skill in the art to practice the applicant's invention, applicant respectfully quotes In re Buchner, 929, F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991), that states a specification need not describe – and best omits—that which is well-known in the art.

The Examiner stated that Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Bu₄I as soluble iodide, does not reasonably provide enablement for any or all iodide generically embraced in the claim language.

In response, applicant respectfully traverses the above rejection and presents the following comments. As above, applicant respectfully suggests that the disclosure of BuI₄ as a working example, and the listing of numerous iodide reagents on page 8 of the specification, satisfy the enablement requirement by providing a more than adequate road map to enable one of ordinary skill in the art to practice the invention without undue experimentation. (See above cited case law and requirements of the MPEP). Applicant also respectfully suggests that it would be mere routine experimentation to one of ordinary skill in the art to practice the invention by using those examples on page 8 of the specification, as guidance to practice the invention with other iodide reagents.

The Examiner stated that Claim 26 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some X, does not reasonably provide enablement for X=OH embraced in the claim language.

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In response, applicant respectfully traverses the above rejection and presents the following comments. Applicant respectfully suggests that one of ordinary skill in the art would recognize OH as a leaving group, much like the leaving groups described on page 9, lines 11-13 (e.g., chlorine, bromine or iodine.) Applicant suggests that these examples satisfy the enablement requirement by providing a more than adequate road map to enable one of ordinary skill in the art to practice the invention without undue experimentation. (See above cited case law and requirements of the MPEP).

Because the applicant has provided examples of oxidation/cyclization reagents and leaving groups, as required by the cited case law above, the specification and claims 1-8 and 26 meet the statutory requirements of 35 U.S.C. Section 112, first paragraph. Armed with this knowledge, one skilled in the art would be able to use the claimed process without undue experimentation. Therefore, Applicant respectfully requests the withdrawal of this rejection.

Claim Rejections - 35 USC § 102

Claims 10-15, 25 and 27 were rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by the following references:

Wang et al. J. Org. Chem. 62: 7288-7294, 1997;
Wang et al. J. Chem. Soc., Perkin Transactions I 10: 1669-1675, 1998;
Wang et al. J. Chem. Soc., Perkin Transactions I 21: 2783-2787, 1995;
Wang et al. J. Chem. Soc., Chemical Communications, 1687-1688, 1994;
Wang et al. Chemical Communications, 4: 363-364, 1997;
and Wang et al. Bioorg. Med. Chem., 6(2): 185-188, 1996.

In response, Applicants have cancelled claims 25-28, reserving the right to pursue claims 25-28 by a divisional application if applicants so desire to do so. In response to the Examiner's anticipation rejection of claim 10, applicant states that the Examiner has not indicated nor articulated to the applicant an anticipation rejection of claim 10. Therefore, applicant cannot respond to an

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anticipation rejection of claim 10 at this time other than stating that claim 10 is novel and unanticipated against any art of record cited by the Examiner.

Accordingly, in light of these comments, applicant respectfully requests the withdrawal of this rejection.

Claim Rejections - 35 USC § 103

The Examiner maintained that Claims 10, 23, 25 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chabala et al EP 0113,570 for reasons of record.

The Examiner stated that Chabala et al. teaches several 5-amino-imidazole compounds for treatment of intestinal coccidiosis in animal, which include compounds claimed in the instant claims herein. The Examiner stated that the instant claims differ from Chabala et al. in requiring specific protecting groups.

In response, applicant's cancellation of claims 25-28, obviates the Examiner's rejection of those claims 25 and 27. However, with regard to the Examiner's rejection of claims 10 and 23, Applicant respectfully traverses the Examiner's rejection and provides the following comments.

Utilizing the **Graham** factors in an obviousness analysis, applicants respectfully suggests that under the first (scope and contents of prior art) and second factor (ascertaining the differences between prior art and claims at issue), a finding of obviousness cannot be made in the present case.

Applicant states that the present invention is not obvious in light of Chabala et al., in that claim 10 is directed to the preparation of a compound of formula III from a compound of formula 4. Chabala et al. do not teach the formation of compound of formula III from a compound of formula 4. Applicant argues that the differences in scope between the present invention and Chabala et al. are such, as not to render claims 10 and 23 obvious to one of ordinary skill in the art. Therefore, applicant respectfully requests the withdrawal of this rejection.

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In view of the foregoing, applicant submits that the application, as amended, is in condition for allowance and courteously solicits a Notice of Allowance.

No fees, other than the fee of \$410.00 for a two month extension of time, are believed to be due with this amendment. If any fees are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from Account No. 19-0365.

If for any reason the Examiner believes that an interview would be helpful to resolve any remaining issues, he is invited to telephone the undersigned at the number listed below.

Respectfully submitted,

SCHERING-PLOUGH CORPORATION



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(908) 298-2161

I hereby certify that this correspondence is being deposited with the United States Postal Service as First class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date of Deposit

4/15/2003

WILLIAM LEE

Registered Representative



Signature

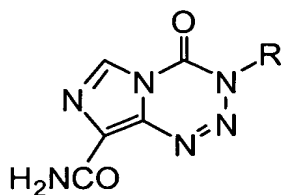
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4/15/2003

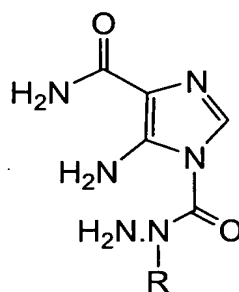
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Version of Claims with Markings
(Amendments highlighted in bold, language to be added underlined,
language to be deleted in brackets)

1. (Amended) A process for the preparation of a compound of the formula IA



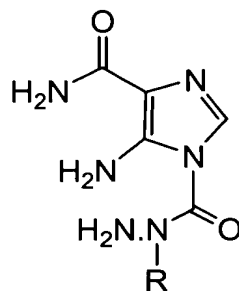
wherein R is an alkyl group having from 1 to 6 carbon atoms, which comprises reacting a compound of the formula II



wherein R is described above, with an oxidation/cyclization agent in the presence of an iodide **compound**, in an inert **[medium] organic solvent**, under an inert atmosphere and at a temperature **[and for a time sufficient enough to produce a compound of the formula IA]**, wherein said iodide is soluble in said inert **[medium] organic solvent, with the proviso that when said oxidation/cyclization agent is not an iodide, the iodide compound itself is the oxidation/cyclization agent.**

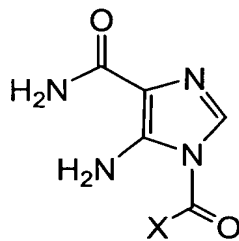
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16. (amended) A process for the preparation of a compound of the formula II:



II

wherein R is an alkyl group having from 1 to 6 carbon atoms, comprising,
reacting a compound of the formula III:



III

wherein X is a leaving group **[of the type that activates its adjacent carbonyl group towards nucleophiles]**, with an alkylhydrazine having from 1 to 6 carbon atoms.